REMARKS/ARGUMENTS

By the present amendment, claims 40, 49, 50, 55 and 57 have been amended and claims 41-44, 46-48, 50, 52-54 and 56 have been deleted rendering claims 40, 45, 49, 51, 55 and 57-58 pending in the application. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. No new matter has been entered by the present amendment and its entry is respectfully requested.

The Official Action dated June 17, 2003 has been carefully considered. It is believed that the amended specification and claims and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Election/Restrictions

We note that the Examiner has maintained his position with respect to the restriction requirement and the claims have been amended to recite the elected embodiments.

Specification/Claim Objections

The Examiner has objected to the disclosure because of several informalities. In response, the disclosure has been amended as requested by the Examiner with one exception. We disagree that the phrase "PCRs" should be changed to "PCR reactions" as the "R" in "PCR" is a short form of the word "reaction". It is common to add a lower case "s" to an abbreviation in order to indicate plural. Consequently, no amendment is necessary.

35 USC §102

The Examiner has objected to claims 40-41 and 43 under 35 USC §102(b) as being anticipated by Westby et al. (*Bioconj. Chem.* (1992) 3, 375-381). We respectfully disagree with the Examiner for the reasons that follow.

The purpose of Westby et al. is to use proricin as a model system to evaluate the possibility of linking the A-chain of ricin to another protein so that a disulfide bond would form between the two components. The linker between the components would then be cleaved by a factor Xa specific protease, resulting in the production of an active toxin which would target diseased cells based on the properties of the other protein moiety (e.g., peptide hormone which binds to specific receptors on diseased cells). Westby et al. also discussed the use of mutant B-chains (i.e., ones which no longer have lectin activity) or the N-terminus of the B-chain to allow for the construction of fusion toxins. Westby et al. does not teach the use of proricin in the treatment of diseased cells, but rather as a means of generating disulfide linked fusion toxins. Claim 40, as amendment, recites a recombinant protein comprising a ricin A chain linked through a cancer associated protease to a ricin B chain. Such a construct is neither disclosed nor suggested in Westby et al. and therefore Westby et al. cannot be said to anticipate the claims.

We also submit that Westby et al. supports the inventiveness of the present claims. In particular, at page 378 the authors indicate that a modified linker may become buried in a fusion protein and/or the cleavage site may become inaccessible by virtue of the novel protease-sensitive cleavage site. The authors further indicate that under the conditions of the experiments reported in the paper, factor X was "generally poor" at recognizing the site in the modified linker region. As is apparent from the discussion in Westby et al. at page 379, the authors were concerned about the impact of the changes required to create a factor X recognition site (even though it was a change of only three amino acid residues). Such a change may have prevented accessibility of the site to the protease; detrimentally affected disulfide bonding between cysteines which flank the linker; or disturbed the normal biological properties of the precursor substrate. In short, Westby teaches that it is not predictable whether a toxin modified with a heterologous linker would in fact be cleaved. Therefore, Westby et. al. can be said to support the inventiveness of the present claims.

We point out that Westby et al. was also cited during prosecution of one of Applicant's other applications, serial no. 09/147,208 (now U.S. Patent No. 6,333,303). In that case, we submitted a Declaration under 37 CFR §1.132 of John Michael Lord who is an expert in this area of technology. A copy of the Declaration is enclosed. We point out that Dr. Lord is the same Dr. Lord who appears as an author on the Westby et al. reference. As will be seen by the enclosed Declaration, Dr. Lord is of the opinion that the claims of the present application are not obvious in view of Westby et al. In view of Dr. Lord's credentials and his first hand knowledge of the cited references, we cannot see how the Examiner can dispute his opinion.

In view of the foregoing, we respectfully request that the objection to claims 40-41 and 43 under 35 USC §102(b) as being anticipated by Westby et al. be withdrawn.

The Examiner has objected to claims 40-41, 43 and 54-58 under 35 USC §102(b) as being anticipated by Borgford (WO 97/41233).

Borgford was published on November 6, 1997 while the present application claims priority date of April 30, 1997. Consequently, since the inventor on both cases is identical, this reference is not available under 35 USC §102(b). We also submit that Borgford relates to recombinant ricin proteins wherein the linker sequence comprises a cleavage site for a viral protease. In contrast, the claims of the present application specify that the linker sequence contains a cleavage recognition site for a cancer associated protease. Consequently, Borgford does not anticipate the present claims.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §102(b) as being anticipated by Borgford be withdrawn.

Obviousness Type Double Patenting

The Examiner has objected to claims 40-41, 43 and 58 under the judicially created doctrine of the obviousness-type double patenting over claims 11 and 19 of U.S. Patent No. 6,531,125 (hereinafter the '125 patent). The '125 patent has the same disclosure

as the Borgford reference cited above under 35 USC §102(b). As mentioned, Borgford relates to recombinant ricin proteins wherein the linker sequence contains a cleavage recognition site for a viral associated protease. The claims as amended herewith specify that the linker sequence contains a recognition site for a cancer associated protease. Consequently, we submit that the claims as currently pending are patentably distinct over Borgford and a terminal disclaimer is not required.

Provisional Rejection-Obviousness Type Double Patenting

The Examiner has also objected to claims 40-41, 43, 45, 47, 49-53 and 59 as conflicting with claims 15, 17, 18, 20, 22, 24, 26 and 40 of Application No. 10/394,511. We note the Examiner's objection and submit that either the overlap will be removed from the co-pending application or a terminal disclaimer will be filed once we receive an indication that the present application is in order for allowance.

We assume that reference to U.S. application no. 09/674,266 on page 7, paragraph 4 of the office action is in error.

The Commissioner is hereby authorized to charge any deficiency in fees (including any claim fees) or credit any overpayment to our Deposit Account No. 02-2095.

In view of the foregoing, we submit that the application is in order for allowance and an early indication to that effect would be greatly appreciated. Should the Examiner like to discuss the matter, he is kindly requested to contact Micheline Gravelle at 416-957-1682 at his convenience.

Respectfully submitted,

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Attachments